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Analysis of Temporal Variability in the Short-term Effects of Ambient Air Pollutants on Nonaccidental Mortality in Rome, Italy (1998–2014)

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Objectives: The association between short-term air pollution exposure and daily mortality has been widely investigated, but little is known about the temporal variability of the effect estimates. We examined the temporal relationship between exposure to particulate matter (PM) (PM_{10}, $PM_{2.5}$) and gases (NO_2, SO_2, and CO) with mortality in a large metropolitan area over the last 17 y.

Methods: Our analysis included 359,447 nonaccidental deaths among ≥35-y-old individuals in Rome, Italy, over the study period 1998–2014. We related daily concentrations to mortality counts with a time-series Poisson regression analysis adjusted for long-term trends, meteorology, and population dynamics.

Results: Annual average concentrations decreased over the study period for all pollutants (e.g., from 42.9 to 26.6 $\mu g/m^3$ for PM_{10}). Each pollutant was positively associated with mortality, with estimated percentage increases over the entire study period ranging from 0.19% (95% CI: 0.13, 0.26) for a 1-Mg/m^3 increase in CO (0–1 d lag) to 3.03% (95% CI: 2.44, 3.63) for a 10-$\mu g/m^3$ increase in NO_2 (0–5 d lag). We did not observe clear temporal patterns in year- or period-specific effect estimates for any pollutant. For example, we estimated that a 10-$\mu g/m^3$ increase in PM_{10} was associated with 1.16% (95% CI: 0.53, 1.79), 0.99% (95% CI: 0.23, 1.77), and 1.87% (95% CI: 1.00, 2.74) increases in mortality for the periods 2001–2005, 2006–2010, and 2011–2014, respectively, and corresponding estimates for a 10-$\mu g/m^3$ increase in NO_2 were 4.20% (95% CI: 3.15, 5.25), 1.78% (95% CI: 0.73, 2.85), and 3.32% (95% CI: 2.03, 4.63).

Conclusions: Mean concentrations of air pollutants have decreased over the last two decades in Rome, but effect estimates for a fixed increment in each exposure were generally consistent. These findings suggest that there has been little or no change in the overall toxicity of the air pollution mixture over time. https://doi.org/10.1289/EHP19

Introduction

The association between air pollution and daily mortality has been widely examined over the past three decades (Analitis et al. 2006; Brunekreef and Holgate 2002; Zanobetti et al. 2003). In particular, the role of particulate matter (PM) <10 and 2.5 μm (PM_{10} and $PM_{2.5}$) and gaseous pollutants such as nitrogen dioxide (NO_2) and sulfur dioxide (SO_2) has been well described (WHO 2013). The epidemiological findings, together with the evidence from toxicology studies, have had an important role in establishing the World Health Organization Guidelines (WHO 2006) and in implementing European Union (EU); and regional-level policies aimed at reducing emissions and concentrations of air pollutants. In more specific terms, directives from 1998/70/EC (October 13, 1998), 2003/17/EC (March 3, 2003) and 2009/30/EC (April 23, 2009) by the European Community changed fuel composition by lowering the limits of sulfur concentration from 150 mg/kg in 1998 to 10 mg/kg in 2009 (Council of the European Union 1998, 2003, 2009). EU policies on vehicles' emissions were gradually updated to the 2009 EURO 5 emission standards that substantially reduced CO, NO_x, and PM_{10} emissions from all newly produced vehicles in comparison with older ones (Council of the European Union 2007). Table S1 displays emission standards for gasoline vehicles, diesel-powered engines, and motorcycles from different stages (Euro 1 to Euro 5). Emissions drop dramatically over time, with different patterns for the different types of vehicles. In addition, some diesel-powered vehicles that appeared to be in compliance with EU standards based on emissions during vehicle testing substantially exceeded the standards during actual use (Franco et al. 2014; Schmidt 2016).

During the decade of the 2000s, national and local governments in Rome, Italy, offered monetary incentives to consumers with the aim of modernizing the car fleet and decreasing vehicle emissions. The number of EURO 0 vehicles (built before any emission standards were set) and EURO 1 vehicles (built to meet emission standards set in the early 1990s) decreased from 907,600 (49% of all vehicles) and 322,187 (17%) units in 2000, respectively, to 194,605 (10%) and 55,744 (3%) in 2014, respectively (data provided by the Automobile Club Italy, http://www.aci.it/). In contrast, the proportion of diesel vehicles has substantially increased over time [from 345,148 (14%) units in 2000 to 1,067,583 (42%) in 2014]. Similarly, a large number of motorcycles are now in circulation (having increased from 201,876 units in 2000 to 398,104 in 2014) (see Table S2). These opposing trends in circulating vehicles have probably contributed to a change in the PM composition (Cui et al. 2016), with potential varying health effects for a fixed number of pollutant exposures.

A small number of studies has investigated long-term temporal changes in air pollution concentrations and their relationship with health (Dominici et al. 2007; Fischer et al. 2011). A German study evaluating the short-term effects of PM and ultrafine particles (UFP) on mortality during the period 1992–2002 did not find evidence of decreasing associations over time (Breitner et al. 2009). A U.S. investigation evaluated the health effects of PM on mortality during two periods: 1987–1994 and 1995–2000. The authors used a fixed increment of 10 $\mu g/m^3$ to test the hypothesis whether a changing composition in PM in the second period, rather than a decrease in overall concentrations, might have displayed a positive effect on human health. The study found a decrease in PM-related mortality in the second period, suggesting a positive role of air quality regulations (Dominici et al. 2007). In contrast, a study in Switzerland focusing on the role of PM_{10} and NO_2 on daily emergency hospital admissions and mortality did

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not find relevant changes in the associations from 1995 to 2010 for fixed increments of either pollutant (Perez et al. 2015).

In light of these contrasting results, we evaluated temporal changes in the concentrations of the main air pollutants in Rome, Italy, over the last 17 y, and evaluated temporal changes in the estimated short-term effects on daily mortality over the same period. We have hypothesized that modifications in the car fleet and policy measures might have altered the chemical composition and toxicity of air pollutants, with consequences on the health effect estimates. To test this hypothesis, we have expressed the association estimates for fixed increases in the pollutants.

Methods

Study Population

We conducted the study in Rome, the largest city in Italy, from 1 January 1998 to 31 December 2014. The city of Rome has as a population of 2,863,322 residents [as of 1 January 2014, from the Italian National Institute of Statistics (ISTAT), www.istat.it]. We considered 359,447 deceased residents, ≥ 35 y old at the time of death, who died in the city from nonaccidental causes [*International Classification of Diseases, Ninth Revision* (ICD-9 codes 0–799)] (WHO 1978). We collected daily mortality data from the Regional Register of Causes of Deaths.

Environmental Data

We obtained hourly mean concentrations of PM_{10}, $PM_{2.5}$, NO_2, SO_2 and CO from the Regional Environmental Protection Agency of the Lazio region (www.arpalazio.gov.it). Data were limited to suburban monitors (vs. traffic-pollution monitors that might overestimate exposures) (Gandini et al. 2013) that were active throughout the study period (1998–2014 for NO_2, SO_2, and CO; 2001–2014 for PM_{10}; and 2006–2014 for $PM_{2.5}$) and had $\geq 75\%$ yearly data coverage (Katsouyanni et al. 1996). Because of the long time-series needed for this analysis, only three fixed monitors were eligible for PM and NO_2, two for CO, and one for SO_2. Missing values for a given pollutant on a specific day and monitor were imputed as the average of all measured values of that pollutant on that day from the other monitors, weighted by the ratio of the yearly average for the monitor over the yearly average for all other monitors (Stafoggia et al. 2010).

The Italian Air Force Meteorological Service (www.meteoam.it) provided information on daily temperature, humidity and barometric pressure, that we have used as daily averages in the analyses. Apparent temperature (AT) was calculated from air temperature and dew-point temperature, a proxy of relative humidity (Steadman 1979). AT is an index of human discomfort, defined as a person's perceived air temperature, and this index has been calculated by using the following formula: $AT = -2.653 + (0.994 \times Ta) + (0.0153 \times Td^2)$, where Ta is air temperature and Td is dew point temperature (O'Neill et al. 2003).

Statistical Analysis

We performed a time-series analysis with the daily death count as the outcome variable and with each pollutant in turn as the main exposure. An over-dispersed Poisson regression was applied, controlling for time-varying confounders. Specifically, we chose the following terms as *a priori* confounders: time-trend of mortality, warm and cold temperatures separately, barometric pressure, influenza epidemics, and indicator variables accounting for population depletion during vacation and summer periods. We adjusted for long-term trends and seasonality by adding to the model a three-way interaction term of year, month, and day of the week. This method has been demonstrated to be equivalent to a case-crossover design with "time-stratified" approach for selecting control days (Levy et al. 2001), and simulation studies have shown it to induce minimum bias under a wide range of different scenarios of data-generating processes (Janes et al. 2005a, 2005b). We adjusted for warm temperatures by modeling mean apparent temperature on the same day and previous day (lag 0–1). We have used linear and quadratic terms for days with AT above the overall median, while AT was kept constant to the median value on days below (Faustini et al. 2013; Mallone et al. 2011). Similarly, we adjusted for cold temperatures by modeling the mean temperature of the previous six days (lag 1–6) with a linear term for days below the median, and the variable was kept constant to the median value on days above. We modeled barometric pressure with linear and quadratic terms of the same day (lag 0) variable. We adjusted for influenza epidemics by modeling an indicator variable (coded as 1 for days during peak incidence periods, up to a maximum of 3 consecutive wk within each year, and 0 otherwise), based on weekly incidence data for the city of Rome provided by the National Health Service Sentinel System (Del Manso et al. 2015; Touloumi et al. 2005). Finally, we modeled an indicator variable for holidays (assigned a value of 1 on national and city holidays and 0 on other days), and a three-level variable to account for population shifts during the summer (assigned a value of 2 for days during the 2-wk holiday period in mid-August, 1 for all other days during the period July 16–August 31, and 0 otherwise) (Stafoggia et al. 2009a, 2010).

Once the adjustment model was defined, we added each pollutant in turn to estimate the overall association between daily concentrations of air pollutants and risk of natural mortality. Pollutants were modeled as linear terms at different lags to estimate immediate (lag 0–1), delayed (lag 2–5), and prolonged (lag 0–5) effects. In each case, we used the average of daily concentrations of the pollutant over multiple lag days as the cumulative exposure estimate. All results are expressed as the percentage difference in mortality (with 95% confidence intervals) relative to a fixed increment of each pollutant: 10-$\mu g/m^3$ increases in PM_{10}, $PM_{2.5}$, and NO_2; $1\ \mu g/m^3$ in SO_2; and $1\ Mg/m^3$ in CO. To facilitate comparisons of the magnitudes of associations across the individual pollutants, we also report association with interquartile range (IQR) increases in each pollutant.

To quantify temporal changes in mortality–pollutant associations we modeled interaction terms between daily pollutant concentrations and the year of death, using the lag structure for each pollutant that had the strongest association with mortality in the overall analysis. We tested for heterogeneity among the resulting year-specific estimates by comparing the fit of models with and without the interaction terms.

Because yearly estimates might be unstable due to limited statistical power, we also performed a stratified analysis of four periods: 1998–2000, 2001–2005, 2006–2010, and 2011–2014. The choice of the periods was to facilitate comparisons with estimates reported for the sa2011 to 2014me time periods by previous studies (Stafoggia et al. 2009b; Alessandrini et al. 2013). Because the purpose of this analysis was to test our study hypothesis of potential changes in toxicity of air mixture over time, estimates were reported as mortality differences per fixed increments in each pollutant.

As sensitivity analysis, we also performed stratified analyses of exposures and outcomes during overlapping 3-y intervals throughout the study period. For example, we used separate models to estimate associations between NO_2 and mortality during the periods 1998–2000, 1999–2001, 2000–2002, and so on, up to 2012–2014. In contrast with the interaction term models used to estimate associations for each individual year, the stratified

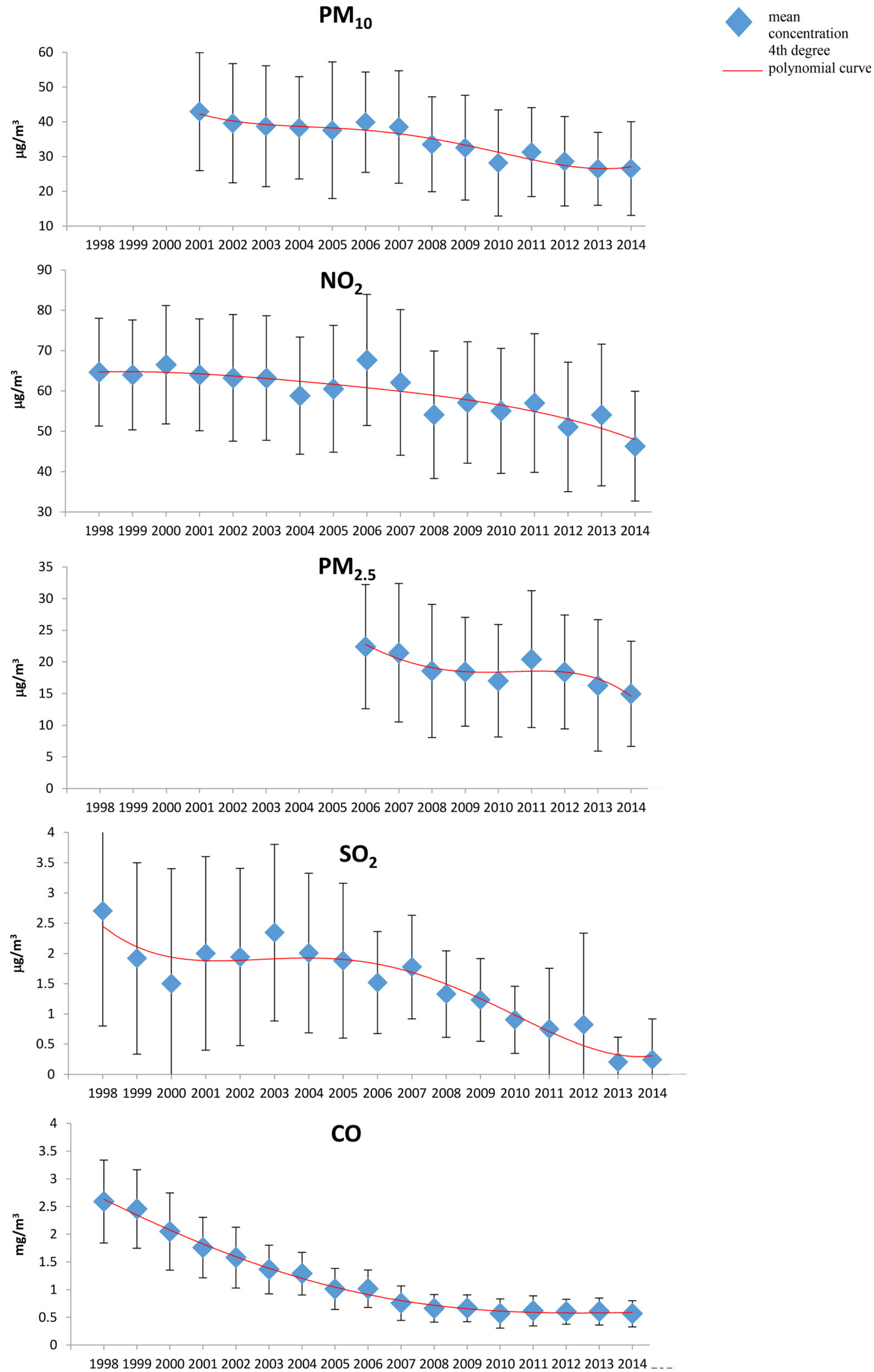

Figure 1. Annual average of daily mean concentrations (standard deviation) of PM_{10} (2001–2014), NO_2 (1998–2014), $PM_{2.5}$ (2006–2014), SO_2 (1998–2014) and CO (1998–2014).

models allowed us to account for time-varying confounders defined for each 3-y period.

Moreover, we performed a meta-analysis of the single-year estimates to evaluate possible sources of variability. We compared heterogeneity explained (I^2) by the original (overall) model and by several meta-regressors of the current and previous year: mean temperature, cold and hot temperature, proportion of elderly people (>65 y old) in the population [provided

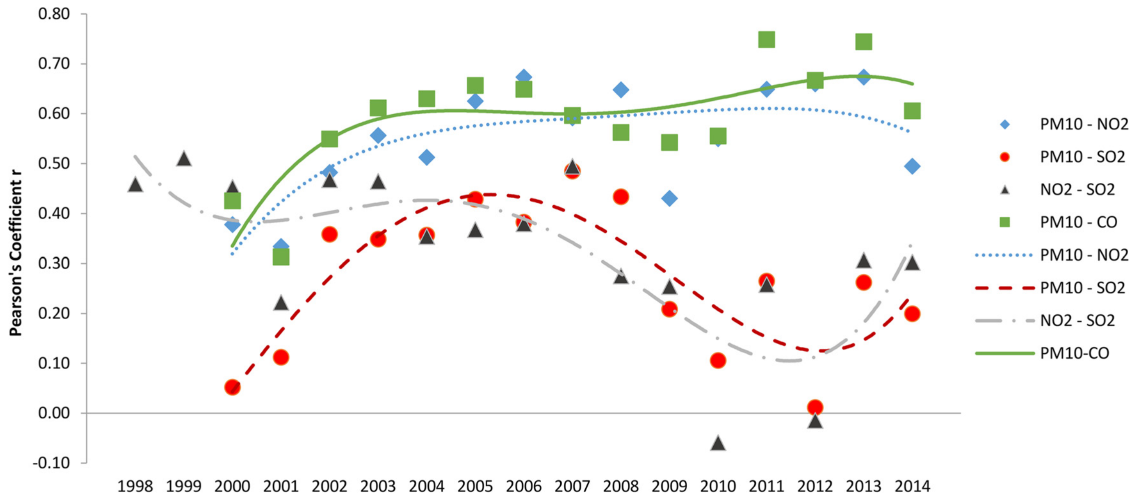

Figure 2. Correlation between pairs of pollutants, by year. See Table S3 for numeric data for all pairwise comparisons.

by ISTAT (www.demo.istat.it)], and annual mean concentration of each pollutant. We used separate models to estimate the heterogeneity explained by each individual meta-regressor, and a single model including all of the variables to derive an overall estimate.

All the analyses were conducted with R software (version 3.1.3; R Development Core Team) and STATA (version 13; R Development Core Team).

Results

A summary of mortality counts and environmental variables during the study period is reported in the online material (see Table S3). Annual averages of daily mean concentrations for each pollutant are displayed in Figure 1. All air pollutants decreased over time. From 1998 (2000 for PM_{10} and 2006 for $PM_{2.5}$) to 2014, annual average concentrations of PM_{10}, $PM_{2.5}$, NO_2, CO and SO_2 dropped by 45%, 33%, 28%, 78%, and 90%, respectively.

Yearly correlations between pairs of pollutants are displayed in Figure 2 and in Table S4. PM_{10} displayed high and stable correlations with both NO_2 and CO over the entire period, with Pearson's correlation coefficients almost always in the range of 0.4–0.7, with no apparent time trends. In contrast, SO_2 showed a weak or null correlation with all other pollutants.

Associations over the full study period for PM_{10}, $PM_{2.5}$, NO_2, and SO_2 were strongest for the 6-d window (lag 0–5), with estimated percentage differences in mortality of 1.46% (95% CI: 0.95, 1.96), 1.75% (95% CI: 0.87, 2.64), and 3.03% (95% CI: 2.44, 3.63) per 10-$\mu g/m^3$ increase in PM_{10}, $PM_{2.5}$, NO_2, respectively, and 2.36% (95% CI: 1.61, 3.11) for a 1-$\mu g/m^3$ increase in SO_2 (Table 1). In contrast, associations between mortality and CO were strongest for lag 0–1 (0.19%; 95% CI: 0.13, 0.26 for a 1-Mg/m^3 increase). We also report estimates per IQR increases in each pollutant, with the unique purpose of comparing associations across pollutants. Mortality differences were higher for NO_2 than PM_{10} and $PM_{2.5}$, with estimates of 7.26% (5.83, 8.71), 2.56% (1.60. 3.52) and 1.92% (0.95, 2.90) per increases of 23.5 $\mu g/m^3$, 18.0 $\mu g/m^3$, and 11.0 $\mu g/m^3$ in lag 0–5 NO_2, PM_{10}, and $PM_{2.5}$, respectively.

Marked variability was seen in year-to-year effect estimates for all pollutants (heterogeneity $p < 0.05$ for NO_2 and $PM_{2.5}$), with relatively strong associations estimated for several pollutants during some years (e.g., for SO_2, NO_2, and CO in 2001), and associations were consistently negative (albeit nonsignificant) during other years (e.g., in 2010) (Figure 3A). In general, no consistent trends were observed in annual associations over time. Estimates for overlapping 3-y periods showed less variation

Table 1. Association between air pollutants and nonaccidental mortality in Rome, Italy: percent difference of risk (% diff), and 95% confidence intervals (95% CI), per fixed and interquartile range (IQR) increases in the pollutants: PM_{10} (2001–2014), $PM_{2.5}$ (2006–2014), NO_2, SO_2 and CO (1998–2014).

		Fixed increase		IQR increase	
Pollutant	Lag (days)	Unit ($\mu g/m^3$)	% Diff (95% CI)	Unit ($\mu g/m^3$)	% Diff (95% CI)
PM_{10}	0–1	10	1.33 (0.93, 1.73)	18.0	2.38 (1.62, 3.15)
	2–5		0.83 (0.40, 1.26)		1.44 (0.63, 2.25)
	0–5		1.46 (0.95, 1.96)		2.56 (1.60, 3.52)
$PM_{2.5}$	0–1	10	1.30 (0.62, 1.97)	11.0	1.43 (0.68, 2.17)
	2–5		1.16 (0.46, 1.87)		1.28 (0.51, 2.06)
	0–5		1.75 (0.87, 2.64)		1.92 (0.95, 2.90)
NO_2	0–1	10	1.80 (1.35, 2.25)	23.5	4.27 (3.19, 5.35)
	2–5		2.13 (1.63, 2.63)		5.07 (3.88, 6.27)
	0–5		3.03 (2.44, 3.63)		7.26 (5.83, 8.71)
SO_2	0–1	1	0.98 (0.50, 1.47)	1.7	1.67 (0.85, 2.50)
	2–5		1.61 (1.00, 2.22)		2.75 (1.70, 3.81)
	0–5		2.36 (1.61, 3.11)		4.04 (2.76, 5.34)
CO	0–1	1*	0.19 (0.13, 0.26)	1.0*	0.20 (0.14, 0.26)
	2–5		0.07 (0.03, 0.11)		0.07 (0.03, 0.11)
	0–5		0.12 (0.07, 0.17)		0.12 (0.07, 0.17)

Note: Poisson regression model adjusted for time trend (three-way interaction between year, month, and day of week), warm temperatures (linear and quadratic terms of hot apparent temperature lagged 0–1 day), cold temperatures (linear term of cold temperature lagged 1–6 d), population summer decrease, holidays, and influenza epidemics (categorical variables), barometric pressure (linear and quadratic term of mean pressure, lag 0).
*Mg/m^3.

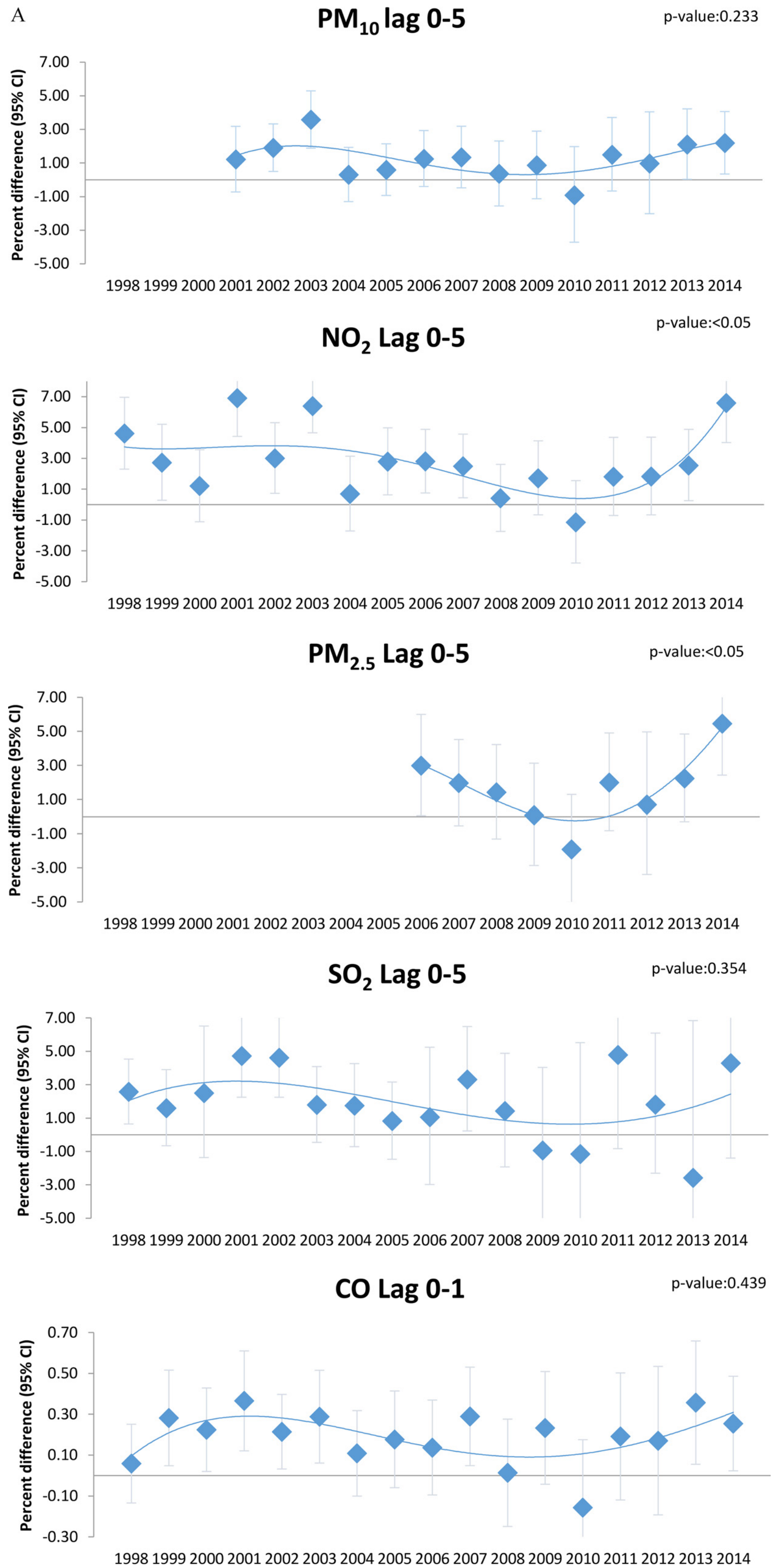

Figure 3. (*A*) Association between pollutants and mortality in Rome, by year (blue dots): percent difference of risk (% Diff), and 95% Confidence Intervals (95% CI) per fixed increases in the pollutants: PM_{10} (2001–2014), $PM_{2.5}$ (2006–2014), NO_2, SO_2 and CO (1998–2014). *p*-Value of the heterogeneity test on annual estimates. (*B*) Association between pollutants and mortality in Rome, by 3-y periods estimates (red squares): percent difference of risk (% Diff), and 95% confidence intervals (95% CI) per fixed increases in the pollutants: PM_{10} (2002–2013), $PM_{2.5}$ (2007–2013), NO_2, SO_2 and CO (1999–2013).

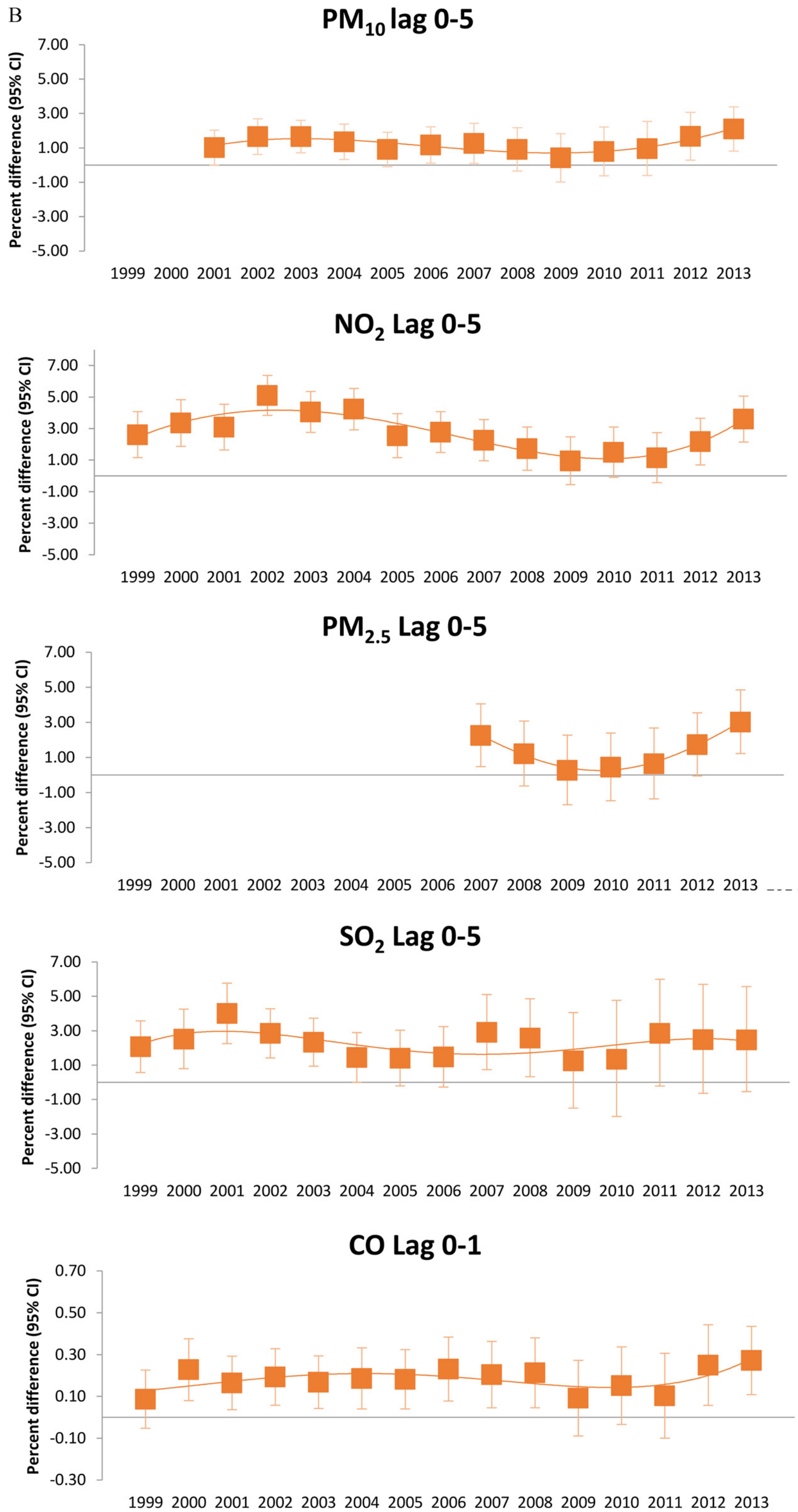

Figure 3. (Continued)

from year-to-year, but also indicated no consistent trends over time (Figure 3B).

Results of meta-analysis of year-to-year estimates showed that PM_{10}, CO, and SO_2 displayed no heterogeneity across years, and this result did not change when meta-regressors were added in the second stage, with a maximum I^2 of 29.0, 10.7, and 8.7, respectively (see Table S5). Instead, NO_2 displayed a large heterogeneity with an I^2 of 72.0 in the single model, but none of the considered meta-regressors can explain it. Finally, extreme temperatures (especially cold ones) seemed to explain most of the heterogeneity in the yearly $PM_{2.5}$ effects on natural mortality as the I^2 dropped from 38.8 to 6.0. Period-specific estimates stratified by time period were generally consistent with the main analysis (Table 2). Apart from NO_2, associations were strongest for the most recent time period (2011–2014), but no consistent trends over time were found.

Discussion

In this study, we described air pollution concentrations in Rome from 1998 to 2014 and estimated their short-term effects on daily mortality. Mean concentrations of all pollutants decreased over the study period, with 2014 annual means being 90% (for SO_2) and 28% (for NO_2) lower than values for 1998. We did not see a clear temporal pattern in the short-term health effects of air pollutants, when expressed per fixed increases over the entire study period.

Downward trends in annual air pollution concentrations have been observed already in other European countries. Querol et al. (Querol et al. 2014) showed a clear decreasing trend in PM_{10}, $PM_{2.5}$, NO_2, SO_2 and CO in Spain from 2001 to 2012. Similarly, Guerreiro et al. (2014) analyzed data for all EU-member states from 2002–2011 and found that air pollutants decreased substantially in all areas. Recently, the European Environmental Agency (EEA) described the same phenomenon over the period of 1997–2010 (EEA-JRC 2013). In Rome, the largest decreases were for SO_2 and CO. These pollutants are known to be produced largely by combustion processes (Bocola and Cirillo 1989), with traffic being their primary source in the Rome metropolitan area. It is possible that the new EU policies had a direct effect on their emission sources. On the other hand, PM and NO_2 decreased less than SO_2 and CO did. One reason might be that the substantial increase in the number of diesel vehicles and motorcycles in Rome has offset decreases in NO_2 emissions and the secondary formation of PM resulting from more stringent limits on emissions from gasoline-powered passenger cars, thereby limiting the potential benefits of the most recent EU policies.

The present study confirmed the consolidated epidemiological evidence on the short-term effects of PM and gases on mortality (Samoli et al. 2006; Zanobetti and Schwartz 2009). We estimated 1.46% (95% CI 0.95–1.96) and 1.75% (95% CI 0.87–2.64) increased mortality per 10-$\mu g/m^3$ increase in lag 0–5 PM_{10} and $PM_{2.5}$, respectively. A recent study of mortality in southern European countries reported slightly stronger effect estimates for 10-$\mu g/m^3$ increases in PM_{10} and $PM_{2.5}$ than corresponding estimates for other European countries or the U.S. (Samoli et al. 2013; Zanobetti and Schwartz 2009).We estimated relatively strong associations with NO_2 over a 6-d period, with an estimated increase in nonaccidental mortality of 3.03%. This estimate is consistent with other Italian multicity studies that applied the same exposure contrast (Alessandrini et al. 2013; Chiusolo et al. 2011; Stafoggia et al. 2009b) and larger than those in other geographical settings. A systematic review collected results from Europe and the U.S. (Mills et al. 2015) and estimated a pooled increased risk in short-term, natural mortality of 0.71% (0.43–1.00) for 10 $\mu g/m^3$ NO_2 (lag 0).

Table 2. Association between air pollutants and nonaccidental mortality in Rome by calendar periods: percent difference of risk (% diff), and 95% confidence intervals (95% CI), per fixed increases in the pollutants: PM_{10} (2001–2014), $PM_{2.5}$ (2006–2014), NO_2, SO_2 and CO (1998–2014).

Pollutant	Period	Unit ($\mu g/m^3$)	% Diff (95% CI)
PM_{10}	2001–2005	10	1.16 (0.53, 1.79)
	2006–2010	10	0.99 (0.23, 1.77)
	2011–2014	10	1.87 (1.00, 2.74)
$PM_{2.5}$	2006–2010	10	1.47 (0.05, 2.91)
	2011–2014	10	2.59 (1.04, 4.16)
NO_2	1998–2000	10	2.61 (1.16, 4.07)
	2001–2005	10	4.20 (3.15, 5.25)
	2006–2010	10	1.78 (0.73, 2.85)
	2011–2014	10	3.32 (2.03, 4.63)
SO_2	1998–2000	1	2.06 (0.57, 3.57)
	2001–2005	1	2.39 (1.30, 3.50)
	2006–2010	1	2.22 (0.35, 4.11)
	2011–2014	1	3.05 (0.33, 5.84)
CO	1998–2000	1*	0.09 (−0.05, 0.23)
	2001–2005	1*	0.19 (0.09, 0.30)
	2006–2010	1*	0.18 (0.06, 0.31)
	2011–2014	1*	0.25 (0.11, 0.40)

Note: Poisson regression model adjusted for time trend (three-way interaction between year, month, and day of week), warm temperatures (linear and quadratic terms of hot apparent temperature lagged 0–1 d), cold temperatures (linear term of cold temperature lagged 1–6 d), population summer decrease, holidays, and influenza epidemics (categorical variables), barometric pressure (linear and quadratic term of mean pressure, lag 0). *Mg/m^3.

Our results regarding yearly or period-specific associations for fixed increments showed no clear patterns over time. When we tested for the presence of heterogeneity in yearly specific estimates, results were inconsistent, and we were unable to identify a significant linear trend. In general, our findings were not consistent with any long-term trend in air pollution–related mortality or with large year-to-year variability. There was less year-to-year variability in stratified estimates based on overlapping three-year periods, but overall temporal variability was similar.

Several studies have hypothesized that the air pollution–mortality association might have changed over long periods because of green air quality policies. A study conducted by Breitner et al. (Breitner et al. 2009) in Germany evaluated the change in mortality risk from 1991 to 2002 using a constant exposure contrast over time, based on the IQR computed on the distribution over the entire study period. They found evidence of decreased risk over the second period (1995–2002) when the concentrations of pollutants were drastically lower as a result of the combination of EU and local policies by the German government. Similarly, Dominici et al. (2007) investigated the role of PM_{10} and $PM_{2.5}$ on the risk of mortality from 1987 to 2000 in the U.S. using a different approach. They analyzed two periods separately, 1987–1994 and 1995–2000, to evaluate whether green policies on emission regulations might have had a possible beneficial impact on human health in the United States. The results underscored a significant effect of PM on mortality risk in the whole period and a suggestive though small decreasing trend from the first to the second period (from 0.21% [0.10, 0.32] to 0.18% [0.00, 0.35] for a fixed increment of 10 $\mu g/m^3$). Other studies reported contrasting results. Perez et al. (2015) found that the association between PM_{10}, NO_2 and health endpoints (mortality and hospital admissions) did not change in Switzerland during 2001–2010, though air pollution levels had decreased substantially. Fischer and colleagues (2011) conducted a similar analysis in the Netherlands that showed similar patterns.

Several studies have reported that some PM components and sources are more strongly associated with health endpoints than other PM components and sources, with overall findings suggesting that combustion and traffic-derived constituents are especially harmful to human health (Cakmak et al. 2014; Eeftens et al. 2014). Bell et al. focused on pollutant sources and subsequent changes in the chemical composition of particulate matter and its related health effects (Bell et al. 2014); they found an increase in cardiovascular and respiratory hospital admissions related to specific components of $PM_{2.5}$, such as black carbon, calcium, and road dust. Similarly, Cakmak et al. (Cakmak et al. 2014) explored the relationship between metals contained in $PM_{2.5}$ and acute changes in cardiovascular and respiratory physiology. They reported statistically significant associations of some metals (calcium, cadmium, lead, strontium, tin, vanadium, and zinc) with reduced lung function and increased heart rate. Other studies of both acute and chronic effects of air pollution exposure have reported evidence suggesting that PM from traffic exhaust (especially organic carbon and elemental carbon) is more harmful to human health than PM from other sources (Atkinson et al. 2015; Eeftens et al. 2014; Harkema et al. 2015; Peng et al. 2009). We hypothesized that new policies might have resulted in greater decreases in traffic-derived PM components than other components, thus adding to the beneficial effect resulting from reduced exposures overall. However, contrary to our hypothesis, we found no clear evidence of a decrease in the health effects of air pollutants over the last 20 y. As already mentioned, one possibility is that an increase in PM toxicity due to the increased presence of diesel vehicles and motorcycles in Rome over recent years might have counterbalanced the benefits of overall emission reductions resulting from the new EURO 4 and EURO 5 vehicle standards.

This study presents several strengths and weaknesses. We investigated a long time-series of data, thanks to the availability of standardized and stable data, both on air pollutants' concentrations and mortality counts. Specifically, we collected 17 y of complete monitor-specific data for SO_2, NO_2, and CO; 15 y for PM_{10}; and 9 y for $PM_{2.5}$, providing enough statistical power to detect even minor associations and temporal changes.

Some limitations have to be acknowledged, the most important of which is that we had no temporal data on PM components, which would have allowed us to test the hypothesis of whether particulate composition changed over time, thus affecting its toxicity and related health effects.

Conclusion

Our results support an effect of air pollution on mortality in Rome, Italy, over the last two decades. Although the mean concentrations of all air pollutants decreased substantially, we could not detect a clear time trend in their effects on mortality, suggesting that the effect of a fixed increment of exposure on mortality may not have changed over time. Similar studies are needed in other settings, possibly complemented with temporal data on specific components of the air pollution mixture, to better evaluate changes in the health effects of ambient air pollutants over time.

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